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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/029,372 | 12/21/2001 | Roger A. Sabbadini | 078853-0302 | 3592 |

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| EXAMINER | |
|---|---|
| LEARY, LOUISE N | |
| **ART UNIT** | **PAPER NUMBER** |
| 1655 | |

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/029,372 | SABBADINI, ROGER A. | |
| | Examiner | Art Unit | |
| | Louise N. Leary | 1655 | |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8,15-17 and 19-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,15-17 and 19-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 1-8, 15-17, and 19-28 are pending in this application.

Claims 9-14 and 18 have been cancelled per applicant's amendment filed April 22, 2004.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

I. Claim1-8, 15-17, 19-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cardiovascular or cerebrovascular disease in a mammal via administering a therapeutic agent, does not reasonably provide enablement for preventing cardiovascular or cerebrovascular disease in a mammal by administering an agent as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification provides an adequate disclosure for treating cardiovascular or cerebrovascular disease in a mammal via administering a therapeutic agent but does not provide adequate support for ---preventing--- cardiovascular or cerebrovascular disease in a mammal. None of the methods in the specification describe --preventing— cardiovascular or cerebrovascular diseases. As a result, persons skilled in this art would not be able to use the method claimed to prevent cardiovascular or cerebrovascular diseases because both diseases are almost always associated with aging in mammals. Therefore, the scope of the invention claimed is not commensurate

with ---preventing--- cardiovascular or cerebrovascular disease in a mammal as claimed.

II. Claims 1-8, 15-17, 19-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The original specification does not use the phrase "small molecule" to describe the agents claimed.

Applicants are required to point out the page and line in the specification that provides support.

3. Claims 1-8, 15-17 and 19-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite because the metes and bounds intended for the phrase "small molecules" can not be determined.

Claim 19 is indefinite because it is unclear whether "modulate" stimulates or inhibits the enzyme activity.

Claim 20 is indefinite due to the omission of ingredient(s) other than "an agent" in the "formulation" claimed. It is suggested that applicants describe all ingredients in the

instant "formulation" to distinctly claim the subject matter which applicant regards as the invention.

Correction is required to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> I. (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Chatterjee.

Chatterjee discloses metabolism of sphingolipids in atherosclerosis and vascular biology. Chatterjee specifically discloses "[N-SMase hydrolyzes sphingomyelin into ceramide and phosphocholine. In turn, ceramide or a homologue serves as an important stress-signaling molecule. Interestingly, an antibody against N-SMase can abrogate Ox-LDL- and TNF-alpha-induced apoptosis and therefore may be useful for in vivo studies of apoptosis in experimental animals....Such findings may provide new avenues for therapy for patients with atherosclerosis.]" See the abstract.

> II. (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 20 is rejected under 35 U.S.C. 102(a) as being anticipated by Miyake et al (Biochem and Biophy Res Commun, Vol. 211, No. 2, pages 396-403, (June 15, 1995).

Miyake et al disclose providing mouse cells with ISP-1/myriocin to test whether "...ISP-1/myriocin has an inhibitory effect on the enzyme, serine palmitoyltransferase, which catalyzes the first step of sphingolipid biosynthesis, the condensation of serine and palmitoyl-CoA into ketodihydrosphingosine (see Fig. 1b). *In vitro* serine palmitoyltransferase activity was blocked by ISP-1/ myriocin in a dose-dependent manner (Fig. 3a)." See pages 399-400.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 15-17, 19, and 21-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee, S. (Arterioscler Thromb Vasc Biol., 1998; 18: 1523-1533) in combination with Miyake et al (Biochem and Biophy Res Commun, Vol. 211, No. 2, pages 396-403, (June 15, 1995).

Chatterjee discloses methods that administers an antibody against neutral sphingomyleinase (N-SMase) to experimental animals with atherosclerosis. Chatterjee also reports that "[Such findings may provide new avenues for therapy for patients with atherosclerosis.]" See the abstract. In addition, Chatterjee discloses the structure, biosynthesis, degradation and localization of sphingolipids. Regarding instant claims 2-4, Chatterjee discloses the role of sphingolipids in vascular disease, atherosclerosis and the brain. See pages 1523-1526. Chatterjee discloses the regulation of

sphingoglycolipid metabolism by lipoproteins. See pages 1526-1529. Chatterjee discloses the role of sphingoglycolipids in intracellular signaling. In "Table 2", Chatterjee discloses the roles of sphingosine, sphingosine-1-phosphate, ceramide, galactosylceramide, glucosylceramide, lactosylceramide, globotriosylceramide and lysosphingolipid. Chatterjee also describes intracellular signaling reactions that involve kinase activity. See page 1530. Further, Chatterjee discloses "[Such findings may provide new avenues for therapy for patients with atherosclerosis.]" See the abstract, page 1523. Thus, Chatterjee discloses or suggests the invention claimed except for addressing the selected use of the serine palmitoyl transferase and myriocin or a related enzyme and fumonisin.

However, regarding the selected use of the serine palmitoyl transferase and myriocin , Miyake et al disclose methods that treat mouse cells with sphingomyelinase which resulted in mild cell growth recovery after ISP-1/myriocin-dependent suppression. Specifically, Miyake et al disclose methods for "treatment of cells with sphingomyelinase which converts sphingomylelin to ceramide, resulted in mild cell growth recovery, following ISP-1/myriocin-dependent suppression. This was likely attributable to increased levels of intracellular ceramide." See page 401. Miyake et al disclose a method which administers ISP-1/myriocin to mouse cells to test an inhibitory effect on the enzyme serine palmitoyltransferase. Miyake et al also disclose "...[the enzyme serine palmitoyltransferase catalyzes the first step of sphingolipid biosynthesis, the condensation of serine and palmitoyl-CoA into ketodihydrosphingosine (see Fig. 1b). *In vitro* serine palmitoyltransferase activity was blocked by ISP-1/ myriocin in a dose-

dependent manner (Fig. 3a).]" See pages 399-400. . Regarding the limitations of instant claim 25, Miyake et al disclose fumonisin B1 was tested as an effector in the assay. Note "Table 1" on page 401. Further with respect to the limitations of instant claim 23, Miyake et al disclose threo-dihydrosphingosine was tested as an effector in the assay. Note page 402.

Thus, Chatterjee disclose the invention as claimed except for addressing the selected use of the serine palmitoyl transferase and myriocin or a relative enzyme and fumonisin B1 in the instant methods which was provided by the Miyake et al disclosure before this invention was made.

Therefore, it would have been obvious to one having ordinary skill in this art at the time this invention was made to provide the invention claimed because Chatterjee disclose the invention as claimed except for addressing the selected use of the serine palmitoyl transferase and myriocin or a relative enzyme and fumonisin B1 in the instant methods which was provided by the Miyake et al.

6. Claims 22, 26 and 27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. The Sabbadini et al reference (U.S. Patent No. 6,881,546 B2) has been cited to further show the state of this art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise N. Leary whose telephone number is 571-272-0966. The examiner can normally be reached on Monday to Friday from 10 to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LOUISE N. LEARY
PRIMARY EXAMINER

October 26, 2005